From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

# PCT

## WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

| | |
|---|---|
| Date of mailing *(day/month/year)* see form PCT/ISA/210 (second sheet) | |
| Applicant's or agent's file reference<br>see form PCT/ISA/220 | **FOR FURTHER ACTION**<br>See paragraph 2 below |
| International application No.<br>PCT/CA2004/000375 | International filing date *(day/month/year)*<br>12.03.2004 |
| Priority date *(day/month/year)*<br>02.04.2003 | |
| International Patent Classification (IPC) or both national classification and IPC<br>A61K31/7032, A61P29/00, A61P3/06 | |
| Applicant<br>MTI META TECH INC. | |

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

(Jan 11/05)

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

(Feb 2/05)

For further options, see Form PCT/ISA/220.

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3. For further details, see notes to Form PCT/ISA/220.

| Name and mailing address of the ISA: | Authorized Officer |
|---|---|
| European Patent Office - Gitschiner Str. 103<br>D-10958 Berlin<br>Tel. +49 30 25901 - 0<br>Fax: +49 30 25901 - 840 | Beranová, P<br>Telephone No. +49 30 25901-333 |

**WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY**

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**Box No. I Basis of the opinion**

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was field, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

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**Box No. II Priority**

1. ☒ The following document has not been furnished:

   ☒ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).

   ☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).

   Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

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**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 10-14,19-28

because:

☒ the said international application, or the said claims Nos. 10-14 (with respect to industrial applicability) relate to the following subject matter which does not require an international preliminary examination *(specify)*:

**see separate sheet**

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the whole application or for said claims Nos. 19-28

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form ☐ has not been furnished

☐ does not comply with the standard

the computer readable form ☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

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**Box No. IV Lack of unity of invention**

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has:

   ☐ paid additional fees.

   ☐ paid additional fees under protest.

   ☒ not paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is

   ☐ complied with

   ☒ not complied with for the following reasons:

   **see separate sheet**

4. Consequently, this report has been established in respect of the following parts of the international application:

   ☐ all parts.

   ☒ the parts relating to claims Nos. 1-18

**Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

| | | | |
|---|---|---|---|
| Novelty (N) | Yes: | Claims | 7-9 |
| | No: | Claims | 1-6,10-18 |
| Inventive step (IS) | Yes: | Claims | - |
| | No: | Claims | 1-18 |
| Industrial applicability (IA) | Yes: | Claims | 1-9,15-18 |
| | No: | Claims | - |

2. Citations and explanations

**see separate sheet**

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**Re Item III.**

3.1 Claims 10 - 14 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

**Re Item IV.**

4.1 The separate inventions are:

1) Use of gangliosides for the treatment of inflammation (claims 1-18)
2) Use of gangliosides for reducing plasma cholesterol (claims 19-28)

They are not so linked as to form a single general inventive concept (Rule 13.1 PCT) for the following reasons:

The problem underlying the present application is the treatment of inflammation and lowering plasma cholesterol. The methods of inventions 1 and 2 are different solutions to this problem, their common concept being the use of gangliosides.
The use of gangliosides is already known in the art.

Bucolo et al. (Journal of Ocular Pharmacology, 1993, 9(4), 321 - 332) report that monosialoganglioside isopropyl ester reduces primary signs of allergic inflammation of the eye (page 321, abstract).

EP0351784 relates to isopropyl ester of GM1 ganglioside with anti-inflammatory action and its use for the treatment of systemic, ophthalmic or topical pathologies (claims 1 and 2).

Oliveira and Langone (Neuroscience Letters, 2000, 293, 131 - 134) report that administration of monosialoganglioside (GM1) is neuroprotective and diminishes local inflammation (page 131, abstract).

WO95/20959 teaches about a composition comprising an anti-inflammatory amount of sialic acid or its analogue and a method for treating inflammation (claims 1 and 5).

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GB2289274 relates to sialic acid derivatives and their use for the treatment of chronic inflammation (claim 1; page 7, line 11).

WPI/Derwent abstract (AN 1989-225642 & JP1163125) mentions an anti-inflammatory agent containing sialic acid.

WO90/09185 discloses a method for treating peptic ulcers comprising administration of a ganglioside (GM1 or BD1a,b) (claims 1 and 5).

The documents cited do not represent a comprehensive search for any of the defined inventions and are to be considered only as part of the prior art pertaining to the general idea underlying the present application.

In view of this prior art, the common concept identified above is not novel and the problem underlying the present application can be redefined as the provision of further compositions useful for the treatment of inflammation and lowering plasma cholesterol. If these methods are to be linked so as to form a single general inventive concept then the condition of Rule 13(1) PCT must be met, i.e. there must be a same or corresponding technical feature shared by all compositions identified in claims, which makes up the contribution to the state of the art.

Neither the claims nor the description disclose a technical feature or a technical effect linked thereto shared by all methods identified in claims 1 - 28, i.e. the method of invention 1 relates to the treatment of inflammation whereas the method of invention 2 to lowering of plasma cholesterol.

In summary, in view of the prior art cited above, the inventions 1 and 2 are not so linked as to form a single general inventive concept, i.e. Rules 13(1) and 13(2) PCT have not been fulfilled. As a consequence, the application is considered to relate to at least 2 separate inventions.

The following opinion relates therefore only to invention 1, i.e. claims 1 - 18.

**Re Item V.**

5.1 The following documents are referred to in this communication:

D1 : BUCOLO C ET AL: "EFECTS OF MIPRAGOSIDE ON OCULAR ALLERGIC INFLAMMATION IN THE RABBIT" JOURNAL OF OCULAR PHARMACOLOGY, MARY ANN LIEBERT, INC. NEW YORK, NY, US, vol. 9,

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no. 4, 1993, pages 321-332, XP000570599 ISSN: 8756-3320

D2 : EP 0 351 784 A (FIDIA SPA) 24 January 1990 (1990-01-24)

D3 : OLIVEIRA ALEXANDRE L R ET AL: "GM-1 ganglioside treatment reduces motoneuron death after ventral root avulsion in adult rats" NEUROSCIENCE LETTERS, vol. 293, no. 2, 27 October 2000 (2000-10-27), pages 131-134, XP002286616 ISSN: 0304-3940

D4 : WO 95/20959 A (US ARMY) 10 August 1995 (1995-08-10)

D5 : GB 2 289 274 A (ERBA CARLO SPA ; PHARMACIA SPA (IT)) 15 November 1995 (1995-11-15)

D6 : DATABASE WPI Section Ch, Week 198931 Derwent Publications Ltd., London, GB; Class A96, AN 1989-225642 XP002286617 &; JP 01 163125 A (SHISEIDO CO LTD) 27 June 1989 (1989-06-27)

D7 : WO 90/09185 A (ANGIO MEDICAL CORP) 23 August 1990 (1990-08-23)

5.2 In light of the documents cited in the international search report, the invention as claimed (claims 1 - 6 and 10 - 18) does not appear to meet the criteria mentioned in Article 33(1) PCT, i.e. does not appear to be novel and to involve an inventive step for the following reasons:

Document D1 reports that monosialoganglioside (GM1) isopropyl ester reduces primary signs of allergic inflammation of the eye (page 321, abstract). This document is therefore considered to be relevant for novelty and inventive step of the subject-matter of claims 1 - 6 and 10 - 18.

D2 discloses isopropyl ester of GM1 ganglioside with anti-inflammatory action and its use for the treatment of systemic, ophthalmic or topical pathologies (claims 1 and 2).

D3 reports that administration of monosialoganglioside (GM1) is neuroprotective and diminishes local inflammation (page 131, abstract).

Both D2 and D3 are thus novelty-destroying for claims 1 - 3, 5, 6, 10, 12 and 14 - 18.

D4 relates to a composition comprising an anti-inflammatory amount of sialic acid or its analogue and a method of treating inflammation (claims 1 and 5).

D5 teaches about sialic acid derivatives and their use for the treatment of chronic inflammation (claim 1; page 7, line 11).

D6 mentions an anti-inflammatory agent containing sialic acid (abstract).

Documents D4 - D6 are thus considered to be relevant for novelty of claims 1, 3, 5, 6, 10, 12, 14, 15, 17 and 18.

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Document D7 discloses a method of treating peptic ulcers comprising administration of a ganglioside (GM1 or GD1a,b) (claims 1 and 5). Thus, it destroys novelty of claims 1 and 5.

5.3 Dependent claims 7 - 9, although formally novel, do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of inventive step (Article 33(3) PCT).

5.4 For the assessment of the present claims 10 - 14 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.